Remarks

Claims 1, 4, 10-12, 15, 18-20 and 24-27 were considered in the Final Office action of April 24, 2002. All of the claims stood rejected under 35 U.S.C. § 103. Applicants respectfully request reconsideration and withdrawal of the rejections in light of the amendments and following remarks.

Claims 1, 4, 10-12, 15, 18, 20 and 25 were rejected under 35 U.S.C. § 103(a) as being obvious over Kwok et al., U.S. Patent No. 5,945,283 ("Kwok"), in view of JP 09187277 (abstract, July 22, 1997). Each of those claims, as well as claim 26, were also rejected as being obvious over Kwok in view of Gillespie, U.S. Patent No. 5,482,834 ("Gillespie"). Claim 19 was rejected over Kwok in view of JP 09187277 and Lu. et al., Chung-Hua I Hsueth Tsa Chih (abstract, November 1995) 75 (11): 679-82 ("Lu"). Finally, claim 27 was rejected over Kwok in view of O'Dell et al., Clinical Chemistry (1998) 44 (1): 183-85 ("O'Dell").

Claims 1 and 25, as amended, recite a method for determining the presence of a target nucleotide on a nucleic acid in a biological sample, and specifically recite a dideoxy nucleotide having an attached acceptor molecule that, upon incorporation of said dideoxy nucleotide into a double-stranded nucleic acid product resulting from the primer extension reaction, is proximate to said donor molecule such that said acceptor molecule is activated through fluorescent energy transfer from the donor molecule so as to produce a detectable fluorescent signal without self-quenching.

As discussed in Applicants' response of December 19, 2001, Kwok reports a method for determining the presence of a target nucleotide by adding to a DNA sample a primer covalently labeled with a fluorescent dye and performing primer extension in presence of a dideoxy nucleotide covalently labeled with a fluorescent dye capable of being activated through fluorescent energy transfer to produce a detectable fluorescent signal when the dideoxy nucleotide is incorporated into the extension product. However, according to the disclosure of Kwok, the signal is produced only upon denaturization and release from the hybridization to the target nucleic acid (Kwok, column 6, lines 38-40, column 9, lines 13-17, Figures 1 and 2). Kwok entirely fails to disclose a dideoxy nucleotide having an attached acceptor molecule that, *upon incorporation of said dideoxy*

nucleotide into a double-stranded nucleic acid product resulting from the primer extension reaction, is proximate to said donor molecule such that said acceptor molecule is activated through fluorescent energy transfer from the donor molecule so as to produce a detectable fluorescent signal without self-quenching.

In order to establish a *prima facie* case of obviousness, all the claim limitations must be taught or suggested by the prior art references. See *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

As amended, each of the pending claims recite a dideoxy nucleotide having an attached acceptor molecule that, when incorporated into a double-stranded nucleic acid product resulting from the primer extension reaction, is sufficiently proximate to the donor molecule produce a fluorescent signal without self-quenching. That is to say, the fluorescent signal is detectable on the double-stranded primer extension product, without the necessity of denaturization. Kwok fails to teach such an element. In fact, Kwok teaches away from modifying its disclosure to produce Applicants' invention because Kwok reports that, according to its methods, the fluorescence energy transfer is achieved through hydrophobic interaction between the dye molecules when the single-stranded oligonucleotide is no longer conformationally restrained by the target nucleotide, *i.e.*, when the single-stranded oligonucleotide is free and in solution (Kwok, column 8, line 63 - column 9, line 1). None of JP 09187277, Gillespie, Lu, or O'Dell supply the element missing from Kwok.

Accordingly, Applicants submit that Kwok even if combined with JP 09187277, Gillespie, Lu, or O'Dell, does not teach or suggest all the elements of the claimed invention. As such, Applicants respectfully request that the rejection of the pending claims under 35 U.S.C. § 103 be reconsidered and withdrawn.

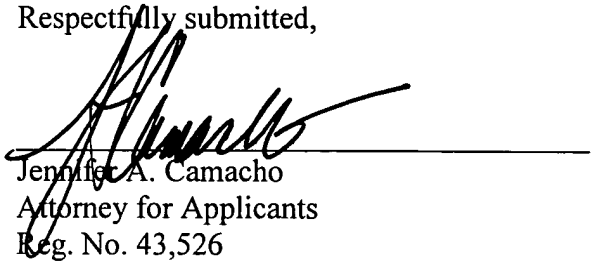
CONCLUSION

Based on the above amendments and remarks, Applicants respectfully submit that pending claims 1, 4, 10-12, 15, 18-20 and 24-27 are in condition for allowance and request entry as such. Applicants believe that no fee is due at the time of submission of

this paper, however, in the event that any fees are due, the Director is hereby authorized to charge any such fees to Attorney's Deposit Account No. 20-0531.

If the Examiner believes that a conversation with Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at the telephone number below.

Respectfully submitted,



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